d) assaying said culture medium for [secreted factors.] said secreted cellular antigens characteristic of said tissue, cells, ascites, or effusion fluid, and indicative of a disease state or lack thereof.

--22. The method according to claim 1 wherein said sensitivity of the cells according to step e) is sensitivity to a wound healing agent.--

REMARKS

The title of the application has been amended, as requested by the Examiner, so that it is clearly indicative of the invention to which the claims are directed. Claims 1, 4-7, 11, 13 and 15-16 have been amended. Claims 2 and 8 have been canceled. Claim 22 has been added. Claims 1, 3-7, and 9-21 remain in the application. Reexamination and allowance of the new and amended claims are requested.

The Examiner provisionally rejected claims 1-21 under 35 U.S.C. § 101 as claiming the same invention as that of claims 1-7 of co-pending Application No. 08/679,056, and as claiming the same invention as that of claims 1-2 of co-pending Application No. 09/095,993. However, the claims of the present application are not directed toward malignant tissue specimens as are the claims of the parent patent and the co-pending application. As amended, the claims of the present application specifically exclude malignant tissue specimens. Therefore, the claims of the present application are not coextensive in scope with the claims of either United States Patent No. 5,728,541 or United States

Patent Application Serial No. 09/095,993. Claim 2 has been canceled because it is directed solely to tumor tissue as is claim 1 of the parent patent.

Claim 6 has been amended, and claim 22 has been added, to refer to specific applications pertaining to non-malignant tissue. Support for the amendment of claim 6 is found on page 6, lines 18 and 22 of the specification. Support for claim 22 is found on page 6, lines 19 and 21 of the specification.

No other pending applications are related to this application.

Accordingly, the rejection of claims 1-21 of the present application for claiming the same invention as United States Patent No. 5,728,541 and United States Patent Application Serial No. 09/095,993 is believed to have been overcome.

The Examiner rejected claims 1-21 under 35 U.S.C. § 102(b) as being anticipated by United States Patent No. 5,242,806 to Yen-Maguire et al. The Examiner maintains that Yen-Maguire et al. discloses assaying for the sensitivity of biopsied tumor cells to chemotherapeutic agents, and the measurement of the responsiveness of multiple cell populations rather than single-cell suspensions (column 3, first full paragraph).

The invention in the present application includes the steps of growing a tissue cell monolayer from a mechanically separated cohesive multicellular particulate, inoculating the cells from the monolayer into segregated sites, treating cells at the segregated sites with one or more treating means and determining the relative effect of the treatment means on the cells, as compared to untreated or differently treated cells.

The Yen-Maguire et al. patent discloses mincing tissue samples to 1 mm. However, the mincing step is to disaggregate the cells for plating. If the mincing step is ineffective to disaggregate the cells from the minced tissue, the tissue is further processed to disaggregate the cells. (See columns 12-13.) Cohesive multicellular particulates are therefore not produced by this method. For this reason, it is believed that claims 1-21 are not anticipated by Yen-Maguire et al.

The Examiner rejected claims 1-21 under 35 U.S.C. § 102(b) as being anticipated by United States Patent No. 4,423,145 to Stampfer et al. The Examiner maintains that Stampfer et al. discloses obtaining clumps of cells from a biopsy, culturing them, and determining adriamycin sensitivity to specimens with varying concentrations. (Column 6, last full paragraph.) However, the tissue samples disclosed by Stampfer et al. are not mechanically separated. In the present application, the tissue samples are mechanically separated. For this reason, it is believed that claims 1-21 are not anticipated by Stampfer et al.

The Examiner rejected claims 1-21 under 35 U.S.C. § 102(b) as being anticipated by United States Patent No. 5,270,172 to Morgan. The Examiner maintains that Morgan discloses the mincing into fragments and culturing of cancer tissue, and the assaying of chemotherapeutic drugs and doses. Although the Morgan patent contains a description of plating tissue particulates into one or more plates and using the plated samples for chemosensitivity assays, it does not describe passaging a

monolayer derived from the particulates. The Morgan patent teaches, instead, the use of cellular suspension. For this reason, it is believed that claims 1-21 are not anticipated by Morgan.

The Examiner rejected claims 1-21 under 35 U.S.C. § 102(b) as being anticipated by United States Patent No. 4,937,187 to Rotman. According to the Examiner, Rotman discloses forming clumps of cells from tumor biopsies, establishing a cell culture, exposing the cell culture to a therapeutic agent and determining the sensitivity of the cells to the agent. Although the Rotman patent contains a description of plating tissue particulates into one or more plates and using the plated samples for chemosensitivity assays, it does not describe passaging a monolayer derived from the particulates. For this reason, it is believed that claims 1-21 are not anticipated by Rotman.

The Examiner rejected claims 10 and 17 under 35 U.S.C. § 112, first paragraph, as being non-enabling. Specifically, the Examiner alleges that the specification does not instruct a person skilled in the art how to perform the wound healing and gene therapy assays.

However, when taken in context, these claims are enabled. The entire purpose of these claimed assays is to determine whether a person skilled in the art could affect the cells cultured through use of gene therapy or wound healing agents. A person skilled in the art would know that the agent being tested is either a gene therapy or wound healing agent selected from the plethora of gene therapy and wound healing agents described in the literature. The treatment would yield

expected results, determined by the nature of the treatment. The treatment method would have already been known to the skilled artisan. If not, there would be no incentive to test the agent in its wound healing or gene therapy capacity. The invention resides in the evaluation of the effect of a treating means on specific cells prepared in a specific manner, not in the selection of agents. Selection of agents to be evaluated does not require any experimentation. Consulting the scientific literature to select candidate agents for experimentation is well within the abilities of the skilled artisan, and need not be described in detail to be enabling. Experimentation follows the selection of agents, and the techniques to be used are described in enabling detail in the specification. Harvesting, separating, growing, inoculating, treating and assessing steps are carried out as claimed in claim 1 and as described in detail in the specification. Accordingly, the claims are not believed to be non-enabling.

The Examiner rejected claims 13-21 under 35 U.S.C. 112, first paragraph, as being non-enabling. Specifically, the claims are rejected for recitation in these claims of the terms "soluble factors", "cellular markers", "cellular factors" and "biological response modifier". The claims have been amended to clarify that the detection of the markers or factors is indicative of a disease state, of a lack of a disease state or of a cell growth characteristic and to indicate that the markers, factors or modifiers are products of or characteristics of the cells. These markers and factors are well-known in the art.

Accordingly, the claims are not believed to be non-enabling.

The Examiner rejected claims 1-21 under 35 U.S.C. § 112, second paragraph, as being indefinite.

In claim 1, "patient cells" has been amended to remove confusion as to what sort of cells are intended.

In claim 1, "cells ascites" has been amended to clarify that two different specimen sources are being referred to.

In claim 1, "said cohesive" has been amended to eliminate the language implying that an antecedent basis is present.

In claim 1, "one active agent" does not appear to be present in the claim.

In claim 1, step (e) has been revised so that a correlating step is present. Support for the amended terminology is found on page 12, line 33 - page 13, line 6.

In claim 1, "assessment" has been replaced by a gerund form.

In claim 1, "in said site" has been replaced with a term having antecedent basis.

Claim 2 has been canceled.

In claim 4, the description of the assessment has revised to indicate that agents are evaluated separately. Support for the amended language is found on page 20, lines 29-37.

In claim 5, "said plurality of active agents" has been replaced with a term having antecedent basis.

In claim 6, "the sensitivity assayed" has been replaced by a term having antecedent basis. Support for the terminology replacing the term not understood is found on page 6, lines 15-25.

With regard to claim 7, the Examiner alleges that "Terasaki" is a trade name. Applicant believes that "Terasaki" is not a trade name. However, "Terasaki" has been removed from the claim without prejudice. The claim has been amended to make use of terminology describing the use of the dispenser. Support for the amended "aliquot delivery" terminology is found on page 10, lines 28-30.

Claim 8 has been canceled.

In claim 11, the alternative language "and/or" has been replaced by language properly reciting the desired alternatives.

Claim 11 has been amended so that the term "ameliorating agent" is no longer present.

In claim 13, "the step of assessment of sensitivity" has been replaced with a term having antecedent basis.

In claim 13, "soluble factors" has been replaced by language indicating that the factors are secreted by cells. Support for the new terminology is found on page 13, line 18.

In claim 15, "cellular factors" has been replaced by language indicating that cellular markers are identified by immunohistochemical processes. Support for the new terminology is found on page 13, lines 29-33.

Claim 16 has been amended so that it is directed to identifying secreted cellular antigens. Support for the new terminology is found on page 13, lines 15-19.

Accordingly, these claims are no longer believed to be indefinite. Therefore, removal of the rejection is requested.

In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration of the rejections is requested. Allowance of claims 1, 3-7 and 9-22 is respectfully requested.

Respectfully submitted,

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